

FIG. 1

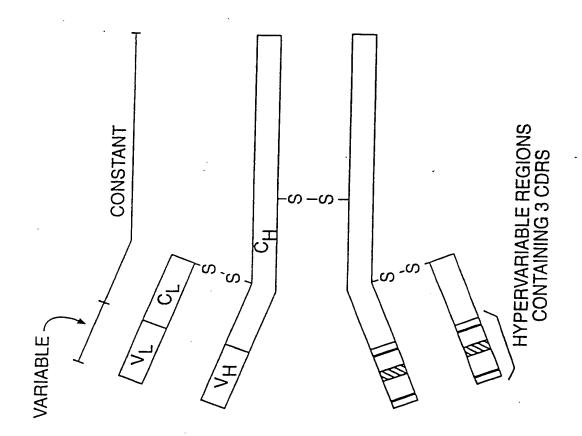


FIG. 2

EFFECT OF ANTI-STAPH MAB 96-110 ON SURVIVAL IN A LETHAL S.AUREUS SEPSIS MODEL

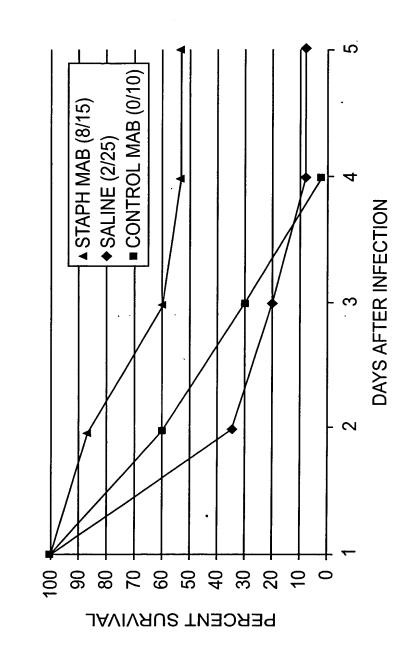


FIG. 3

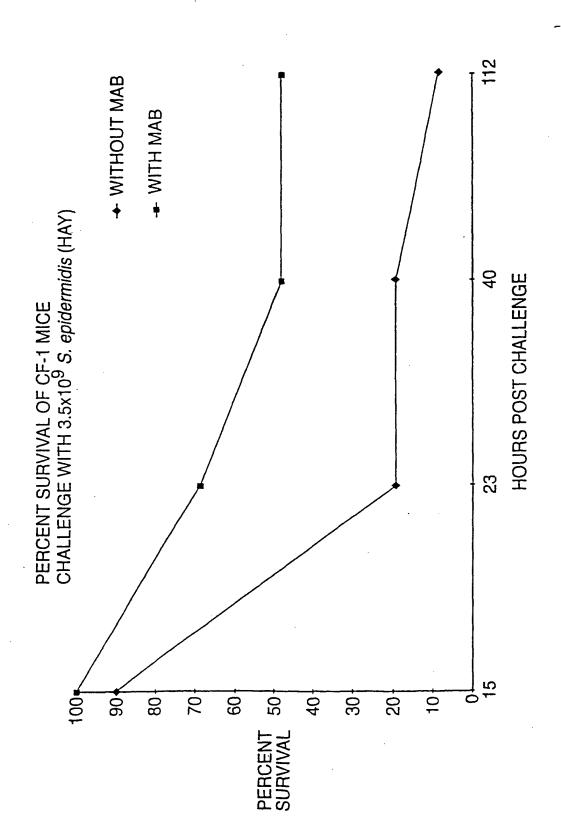


FIG. 4

6MER.SEQ	
	10 20 30
41:13.6mer2-1	GGGGCTCATG CGGATAGGGT TTATGGGGCC SEQ ID NO.4
61	CAHADRVYGA SEQID NO.5
42:14.6mer2-2	GGGGCTCATG CGGATAGGGT TTATGGGGCC
65	GAHADRV Y GA
43:15.6mer2-3	GGGGCTCATG CGGATAGGGT TTATGGGGCC
66	GAHADRV YGA
44:16.6mer2-4	GGGA-TCATG CGGATAGGGT TTATGGGGCC SEQ ID NO.6
62	G ? H A D R V Y G A SEQ ID NO.7
45:17.6mer2-5	GGGGCTCATG CGGATAGGGT TTATGGGGCC
67	GAHADRV YGA
46:18.6mer2-6	GGGGCTCATG CGGATAGGGT TTATGGGGCC
68·	GAHADRV YGA
47:19.6mer2-7	GGGGCTCATG CGGATAGGGT TTATGGGGCC
69	GAHADRVYGA
48:20.6mer2-8	GGGGCTCATG CGGATAGGGT TTATGGGGCC
70 ·	GAHADRVYGA
49:21.6mer2-9	GGGGCTCATG CGGATAGGGT TTATGGGGCC
71	G A H A D R V Y G A
51:23.6mer2-11	GGGGCTCATG CGGATAGGGT TTATGGGGCC
72	G A H A D R V Y G A
52:24.6mer2-12	GGGGCTCATG CGGATAGGGT TTATGGGGCC
73	G A H A D R V Y G A
53:25.6mer2-13	GGGGCTCATG CGGATAGGGT TTATGGGGCC
74	G A H A D R V Y G A
54:26.6mer2-14	GGGGCTCATG CGGATAGGGT TTATGGGGCC
75	G A H A D R V Y G A
55:27.6mer2-15	GGGGCTCATG CGGATAGGGT TTATGGGGCC
76	GAHADRVYGA
56:28.6mer2-16	GGGGCTCATG CGGATAGGGT TTATGGGGCC
77	G A H A D R V Y G A
58:30.6mer2-18	GGGGCTCATG CGGATAGGGT TTATGGGGCC
78	G A H A D R V Y G A
59:31.6mer2-19	GGGGCTCATG CGGATAGGGT TTATGGGGCC
79	G A H A D R V Y G A
60:32.6mer2-20	GGGGCTCATG CGGATAGGGT TTATGGGGCC
80	GAH ADRV YGA

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15MER2.SEQ										(
	10	20	30	40) 		09			
50:07.15mer2-1/0	GGGCTTGGC	ی ا	TCGTATTCCT	AGCTT	CTGCTGGTCG	rggggcc	SEQ .		0.8	
	G A (W)	H W R H	R I P	r o	A A G R	G B	SEQ	ID N	0.9	_
	GGGGCTCGTC	rggT'?	TTTTTCTCAT	LTTCAT	Gercerrcar	TGGGGCC	SEQ	N CI	70.1	0
	G A R (R)(H) G N	$\overline{}$	F (H)	R) S L I	B G	SEQ		10.1	
53:10.15mer2-4/0	GGGCTTCGA	GCTTTGI	TAGTCATTCT	TATCGTCCTC	C GGGGTTCGGC	TGGGCCC	SEQ	101	•	12
73	(M) A D	K) A L (F)	_	조) 교	R G S A	S D	SEQ	ID	_•	[]
54:11.15mer2-5/0	GGGCCTTGGC	TGGCGT	ATT(CAGCT	CTGCTGGTCG	TGGGGCC	SEQ	_		14
74	G A R	ж Ж	H	r ŏ	A A G R	G B	SEQ	ID)		15
56:13.15mer2-7/0	GGGGCTTGGC	'TGGCGT	ATT.	CAGCT	CTGCTGGTCG	TGGGGCC	SEQ	_	_•	16
1.2	G A W	W R	Н	0 L	A A G R	G B	SEQ	_	•	17
57:14.15mer2-8/0	GGGCCTTGGC	TGGCGT	ATT	CAGCT	CTGCTGGTCG	TGGGGCC	SEQ	_	•	18
77	G A W	X X		O C	A A G R	G	SEQ	ID	•	19
58:15.15mer2-9/0	GGGCCTCAGG	SCTGTT	CCT	GCTGAT	CTACTGAGCT	TGGGGCC	SEQ	_	•	30
78	G A D	A V	Д	A D	ATEL	S S	SEQ	_	•	21
59:16.15mer2-10/0	GGGCTCGTC	3ATGGT	TCL	TTTCA5	GGTCGTTCAT	TGGGĜCC	SEQ	_	•	22
79	G A R	e H	လ	H	R S L I	G G	SEQ	111	•	23
60:17.15mer2-11/0	GGGCTCGTC	SATGGT	TCT	TTTCA	GGTCGTTCAT	TGGGGCC	SEQ		•	24
	G A R	R H G N	F S H	H	RSLI	G B	SEQ	101	NO.	25
61:18.15mer2-12/0	GGGCTTGGC	ATGTAT	CAT	GCGCA	Trcgragrcc	TGGGGCC	SEQ		•	26
81	B A S	M		H	(L) R S P	G A	SEQ		•	27
62:19.15mer2-13/0 GGGGCTTG	GGGCTTGGC	ATGTAT	CAT	GCGCA	TICGIAGICC	TGGGGCC	SEQ	II Di	_•	28
82	G A W	M	H	K	L R S P	G B	SEQ		``. 8	29
63:20.15mer2-14/0	GGGCTTGGC	GGAAGTATTT	TAT	gcg	rtgr	TGGGGCC	SEQ	n n	_:	30
83	M C C	M		A	ပ	e C	SEQ	ΠΩ		31
64:21.15mer2-15/0	G	ATGTATT	TCAT	ည္သည္ဟ	TTCGTAGTCC	TGGGGCC	SEQ	ΠΩ	 Q	32
84	G A W	R M Y F		н А н	L R S P	G B	SEQ	OI.	``. S	33
65:22.15mer2-16/0 GGGCCTT	GGGCTTGGC	GTATGTATTT	TTCTCATCGT	CATGCGCATC	TTCGTAGTCC	TGGGGCC	SEQ	OI.	 g	34
85	G A W	RMYF	S H R	H A H	L R S P	GA	SEQ	al	g	35

15MER2.SEQ						
	1	0 20	30	40	50	09
66:23.15mer2-17/0	GGGCTTGGC	GTATGTATTT	TTCTCATCGT	CATGCGCATC	66:23.15mer2-17/0 GGGGCTTGGC GTATGTATTT TTCTCATCGT CATGCGCATC TTCGTAGTCC TGGGGCC SEQ ID NO.36	SEQ ID NO.36
98	M E E	RMYF	S H R	H A H	L R S P G A	SEQ ID NO.37
67:24.15mer2-18/0 GGGCCTCGTC GGCATGGTAA TTTTTCTCAT	GGGGCTCGTC	GGCATGGTAA		TTTTTCATC	GGTCGTTGAT TGGGGCC	SEQ ID
87	G A H	R H G N			R S L I G A	
68:25.15mer2-19/0 GGGGCTTGGC ATTGGCGTCA TCGTATTCCT	GGGCTTGGC	: ATTGGCGTCA	TCGTATTCCT	CTTCAGCTTG	CTGCTGGTCG TGGGGCC	SEQ ID
88	CAM	H W R H	R I P	7 0 T	A A G R G A	SEQ ID
69:26.15mer2-20/0	GGGCTCGTC	: GGCATGGTAA	TTTTTCTCAT	TTTTTTCATC	69:26.15mer2-20/0 GGGGCTCGTC GGCATGGTAA TTTTTCTCAT TTTTTTCATC GGTCGTTGAT TGGGGCC	SEQ ID
89	G A H	R H G N	R H G N F S H	F F H	R S L I G A	SEQ ID

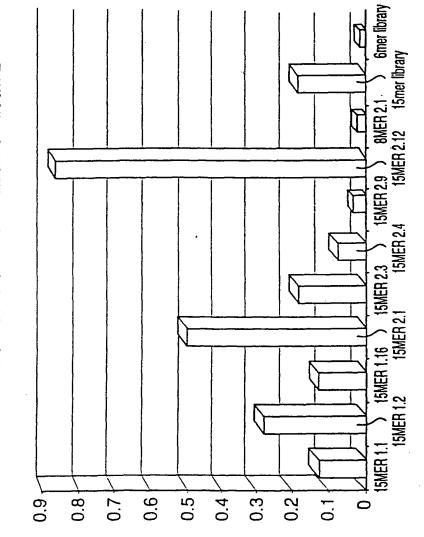
51:28.15mer1-2/0 GGGGCTGATT CGATTACTTT TCATC 6 A D W I T F H 53:32.15mer1-3/0 GGGCTGGTT CGATTACTTT TCATC 6 A D W I T F H 62:13.15mer1-3/0 GGGCTGGTT CGATTACTTT TCATC 6 A D W I T F H 63:14.15mer1-3/0 GGGCTGGTT CGATTACTTT TCATC 6 A D W I T F H 64:15.15mer1-9/0 GGGCTGGTT CGATTACTTT TCATC 6 A D W I T F H 64:15.15mer1-10/0 GGGCTGGTT CGATTACTTT TCATC 6 A D W I T F H 65:16.15mer1-11/0 GGGCTGGTT CGATTACTTT TCATC 6 A D W I T F H 65:16.15mer1-11/0 GGGCTGGTT CGATTACTTT TCATC 70 G G G G G G G G G G G G G G G G G G G
1 I n n n n n n n n n n n n n n n n n n

FIG. 7A

15MER1.SEQ		•			-	
	10	20	30	40	50	09
73:24.15mer1-18/0 GGGGCTGGTT CGATTACTTT TCATCGTCGT CATCATGATC GTGTTCTTTC TGGGGCC	GGGCTGGTT	CGATTACTTT TCATCGTCGT	TCATCGTCGT	CATCATGATC	CATCATGATC GTGTTCTTTC TGGGGC	TGGGGC
74:25.15mer1-19/0 GGGGCTGGTT	GGGCTGGTT		TCATCGTCGT	CATCATGATC	CGATTACTTT TCATCGTCGT CATCATGATC GTGTTCTTTC TGGGGCC	TGGGGCC
78	G A D	WITF	H R R	п н	H H D R V L S G A	Q D
75:26.15mer1-20/0 GGGCTGGT	GGGCTGGTT		TCATCGTCGT	CATCATGATC	CGATTACTIT TCATCGTCGT CATCATGATC GTGTTCTTTC TGGGGCC	TGGGGCC
179	G A D	WITF	H R R	н н	HRRHHDRVLSGA	G A

masterlist	ist					٠				
		10	20	30	40	50		09	07	
51:15mer 1st.1	r 1st.1	GGGGCTGATT	CGATTACTTT	TCATCGTCGT	CATCATGATC	GTGTTCTTTC	TGGGGCC	16/17 S	SEQ ID	NO.5
57		G A D	W I T F	H R R	н н р	R V L S G A	G B	03	EQ ID	NO.5
90 15me	r 1st.2	90 15mer 1st.2 GGGGCTAGTC C	GTCATATGCT	TGCT	TCGCGTTTGC	TTGCTGTTTC I	TGGGGCC	1/10 5	EQ ID	NO.5
91		G A S	R H M L	Ø	SRL	L A V P	ဗ	01	EQ ID	NO.5
71:15me	r 1st.16	GGGCTGGGA	AGGCTATG'IT	_	TATCGTCATC	GGCGTTCGGC	TGGGGCC	1/17 §	SEQ ID	NO.5
85		G A G	K A M F	SHS	Y R H	R G S A	GA	Ç	EQ ID	NO.55
92 15me	15mer 2nd.1	GGGCCTTGGC	ATTGGCGTCA	TCGTATTCCT	CTTCAGCTTG	CTGCTGGTCG	TGGGGCC	5/18 9	SEQ ID	NO.5
98		C A M	H W R H	×	LQL	A A G R	G B	CO	SEQ ID	NO.57
93 15me	15mer 2nd.3	GGGCTCGTC	GGCATGGTAA	TTTTTCTCAT	TT	GGTCGTTGAT	TGGGGCC	6/18		•
66		GAR	R H G N	Ţ	F F H	RSLI	G A	O,	SEQ ID	NO.59
94 15me	15mer 2nd.4	GGGCCTTGGA	AGGCTTTGTT	AGI	TATCGTCCTC	GGGGTTCGGC	TGGGGCC	1/18	SEQ ID	NO.60
100		M W U	N X A L F	S	Y R P	R G S A	G A	Ç	SEQ ID	•
95 15me	15mer 2nd.9	GGGCTCAGG	TGGCTGTTTT	TAT	TTGGCTGATG	CTACTGAGCT	TGGGGCC	1/18	SEQ ID	NO.62
101		G A Q	V A V L	>	L A D	ATEL	G	0,	SEQ ID	NO.6
96 15me	r 2nd.12	15mer 2nd.12 GGGGCTTGGC	GTATGTATTT	Ϋ́	CATGCGCATC	TTCGTAGTCC	TGGGGCC	6/18	SEQ ID	NO.6
		G A W	R M Y F	S H R	H A H	L R S P	A G	0,1	SEQ ID	NO.65
97 6me	6mer 2nd.1	GGGCCTCATG	CGGATAGGGT	TTATGGGGCC				18/18	SEQ II	NO.66
103		G A H	A D R V	Y G A				0,	3EQ 11	NO.67

COMPARISON OF SIGNALS AT 6.25x10" virus/mL



3RD ROUND ISOLATES

FIG. 9

GENERAL CLONING STRATEGY

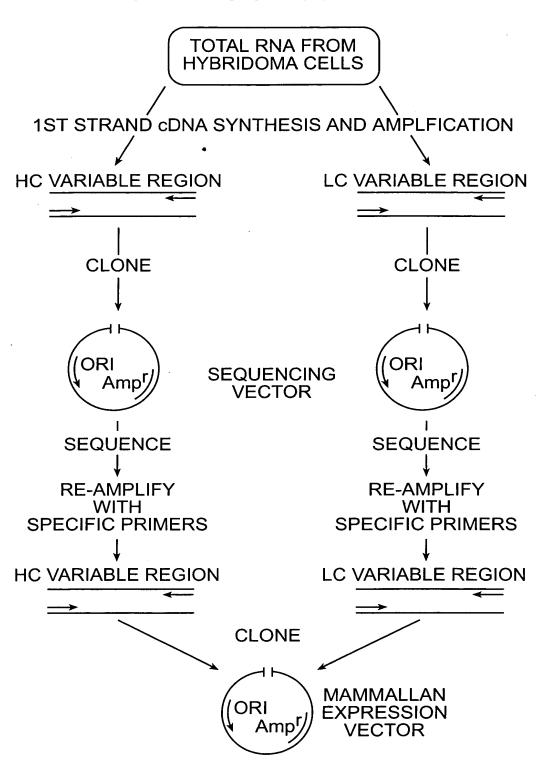


FIG. 10

MOUSE HEAVY CHAIN "FRONT" PRIMERS

SEQ ID NO.68 5'-ATTTCAGGCCCAGCCGGCCATGGCCGARGTRMAGCTKSAKGAGWC-3'

SEQ ID NO.69 5'-ATTTCAGGCCCAGCCGGCCATGGCCGARGTYCARCTKCARCARYC-3'

5'-ATTTCAGGCCCAGCCGGCCATGGCCCAGGTGAAGCTKSTSGARTC-3' SEQ ID NO.70

5'-ATTTCAGGCCCAGCCGGCCATGGCCGAVGTGMWGCTKGTGGAGWC-3' SEQ ID NO.71

5'-ATTTCAGGCCCAGCCGCCATGGCCCAGGTBCARCTKMARSARTC-3' SEQ ID NO.72

MOUSE HEAVY CHAIN "BACK" PRIMERS

JS160

SEQ ID NO.73 5'-GCTGCCACCGCCACCTGMRGAGACDGTGASTGARG-3'

SEQ ID NO.74 5'-GCTGCCACCGCCACCTGMRGAGACDGTGASMGTRG-3' 5'-GCTGCCACCGCCACCTGMRGAGACDGTGASCAGRG-3' SEQ ID NO.75

FIG. 11A

MOUSE LIGHT CHAIN LEADER "FRONT" PRIMERS

5'-CCCGGGCCACCATGGAGACAGACACTCCTG-3' SEQ ID NO.76

5'-CCCGGGCCACCATGGATTTTCAAGTGCAGATTTTC-3' SEQ ID NO.77

5'-CCCGGGCCACCATGGAGWCACAKWCTCAGGTC-3' SEQ ID NO.78

5'-CCCGGGCCACCATGKCCCCWRCTCAGYTTCTKG-3' SEQ ID NO.79

5'-CCCGGGCACCATGAAGTTGCCTGTTAGGCTG-3' SEQ ID NO.80

MOUSE LIGHT CHAIN "BACK" PRIMER

5'-GCACCTCCAGATGTTAACTGCTC-3' SEQ ID NO. 81

"96-110" SPECIFIC PRIMERS

96110HF2

5'-TAATA<u>TCGCGA</u>CAGCTACAGGTGTCCACTCCCGAAGTGATGCTGGTGGAGWCTG-3' SEQ ID NO.82

96100HB 5'-TTATA<u>GAATTC</u>TGAGGAGGGGGGGGGGGG-3' SEQ ID NO.83

96110BLF

5'-TTAGGCGATAGCGTTCTCTCCCAGTCTCC-3' SEQ ID NO.84

96110BLB

5'-GTAACCG TICGAAAAGTGTACTTACGTTTTATTTCCAGCATGGTCC-3' SEQ ID NO.85

FIG. 11B

96-110 ANTI-STAPH (HAY) HEAVY CHAIN VARIABLE REGION (TYPE IIIA)

GAAGTGATGCTGGTGGAGTCTGGTGGAGGATTGGTGCAGCCTAAAGGGTCATTGAAACTCTCATGTGCAGCCTCTGGATTTCACCTTCAAT Ç വ Z; ی വ 口 × Ы വ G × ႕ Ø Λ 7 ט ဗ G ഗ ഥ 口 M N

AACTACGCCATGAAT TGGGTCCGCCAGGAAAGGGTTTGGAATGGGTTGCT

CGCATAAGAAGTAAATAATTATGCAACATTTTATGCCGATTCAGTGAAAGAC R I R S K S N N Y A T F Y A D S V K D AGGTTCACCATCTCCAGAGATGATTCACAAAGCATGCTCTATCTGCAAATGAACAACTTGAAAACCAGAGGACACAGGCCATGTATTACTGTGAGA ď 臼 <u>-</u>-z Z Σ Ø 口 ΙX Σ വ വ Q \Box

CGGGGGGCTTCAGGGATTGACTATGCTATGGACTAC TGGGGTCAAGGAACCTCACTCACCGTCTCCTCA SEQ ID NO. 86 SEQ ID NO. 87 വ လ ⊱ П လ ₽ ტ Ö 3 \succ Ω Σ ø \succ \Box ט വ ď Ö

FIG. 12A

96-110 ANTI-STAPH (HAY) LIGHT CHAIN VARIABLE REGION (TYPE VI)

CAAATTGTTCTCCCCAGTCTCCCAGCAATCCTGTCTGCATCTCCAGGGGAAAAGGTCACAATGACTTGC വ ப ø Д ഗ

AGGGCCAGCTCAAGTGTAAATTACATGCAC R A S S V N Y M H TGGTACCAGCAGAAGCCAGGATCCTCCCCCAAACCCTGGATTTCT GCCACATCCAACCTGGCTTCT Д വ Ö Ŏ GGAGTCCCTGCTCGCTTCAGTGGCAGTGGGTCTGGGACCTCTTACTCTCACAATCAGCAGAGTGGAGGCTGAAGATGCTGCCACTTATTACTGC 四 띠 വ 口 വ വ ₽ ט လ ט വ r വ α Ø

CAGCAGTGGAGTAGTAACCCACCACG TTCGGAGGGGGGACCATGCTGGAAATAAGA SEQ ID NO. 88 Q Q W S S N P P T P G G G T M L E I R SEQ ID NO. 89

CDR REGIONS UNDERLINED

FIG. 12B

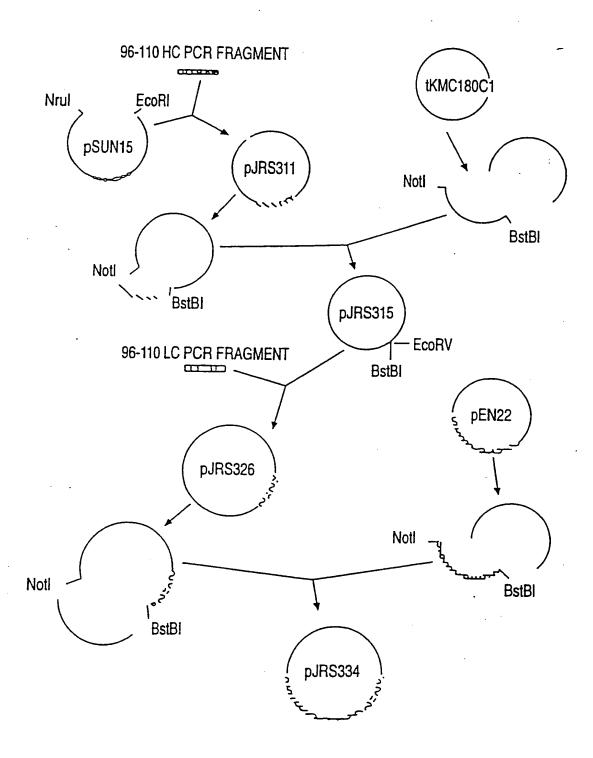
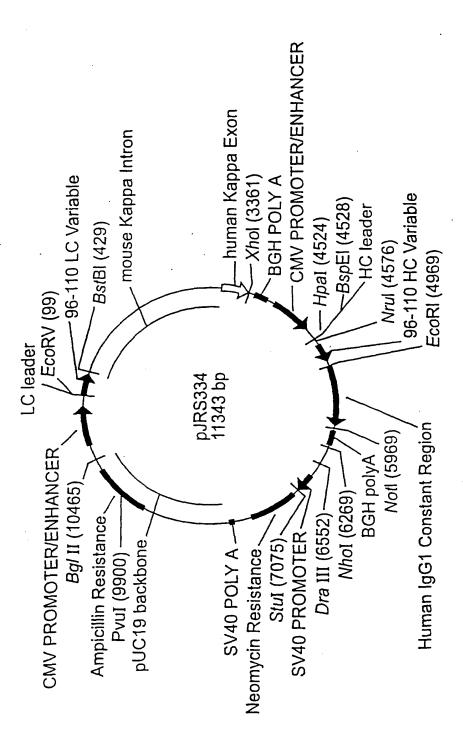


FIG. 13



Common Unique Restriction Sites Shown

FIG. 14

ANTIBODY PRODUCTION ELISA

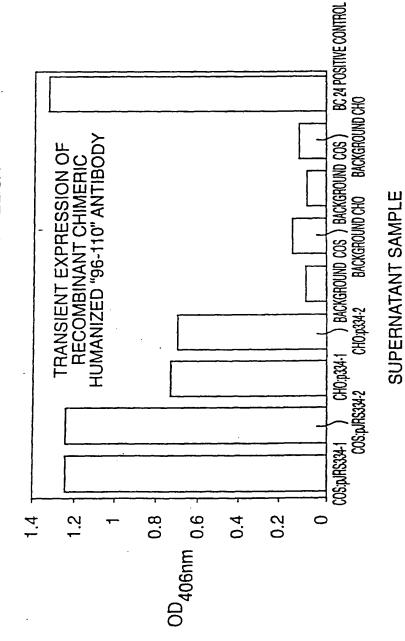


FIG. 15



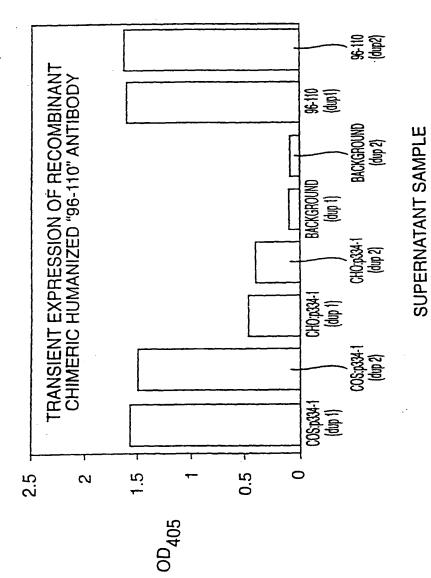
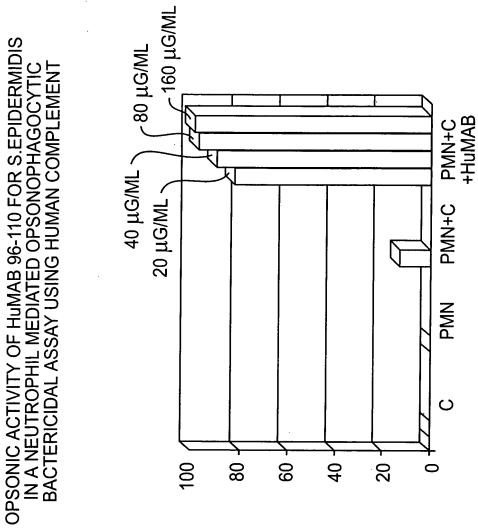


FIG. 16

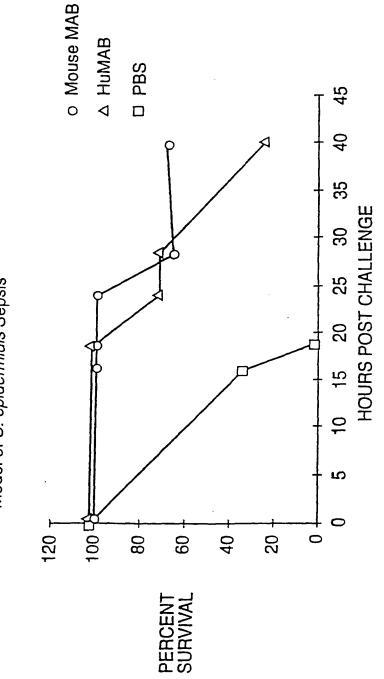


PERCENT BACTERIA KILLED (2HRS)

C- BACK-EX (1:D), HUMAN PMN-HUMAN BACTERIA-S.EPIDERMIDIS (STRAIŅ HAY)

FIG. 17

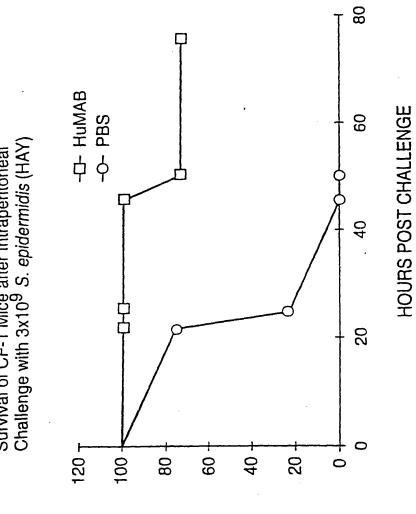
Pilot Study to Compare the Effect of Mouse MAB 96-110 and HuMAB 96-110 in a Lethal Model of S. epidermidis Sepsis



MAB dose: 14 mg/kg given IP, 24 and 1 hour prior to infection

FIG. 18

Survival of CF-1 Mice after Intraperitoneal Challenge with 3x109 S. epidermidis (HAY)



PERCENT SURVIVAL

18 mg/kg/dose, IP, 24 and 1 hour prior to infection

FIG. 19

Effect of HuMAB 96-110 on Bacteremia in a Lethal S. epidermidis Sepsis Model

Geometric Mean Bacteremia Level

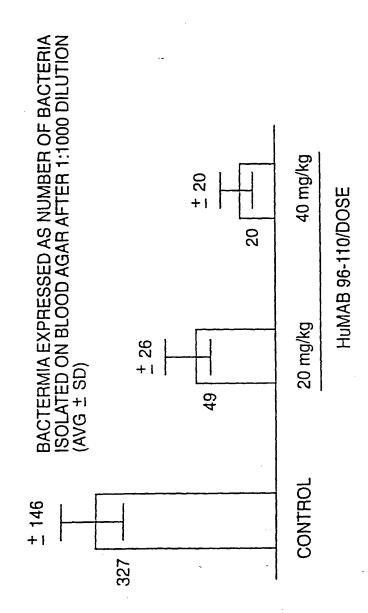
7 × 103	1.7 × 101	18 hrs
5.2 × 104	2.1 x 101	12 hrs
7.2 x 104	7.5 x 102	8 hrs
6.5 x 104	3 x 102	4 hrs
Saline Placebo	HuMAB 96-110	

Time Post Infection

HuMAB 96-110 18 mg/kg/dose or saline given IP, 24 and 1 hour prior to IP infection with 3x109 S. epidermides (Hay)

F/G. 20

BACTEREMIA LEVELS 4 HRS AFTER INFECTION WITH 3X109 S. EPIDERMIDIS*



*CF-1 MICE INFECTED IP WITH STRAIN HAY-HUMAB GIVEN IPx2

FIG. 21

The Effect of Hu 96-110 on Survival in a Lethal Neonatal S. *epidermidis** Sepsis Model

